4 ANSWER 39 OF 123 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:36982 BIOSIS
DOCUMENT NUMBER: PREV199698609117
TITLE: Thiol agents and Bcl-2 identify an alphavirus-induced apoptotic pathway that requires activation of the **transcription factor** NF-kappa B.
AUTHOR(S): Lin, Kuo-I.; Lee, Swu-Hua; Narayanan, Ramaswamy; Baraban, Jay M.; Hardwick, J. Marie; Ratan, Rajiv R. (1)
CORPORATE SOURCE: (1) Johns Hopkins Univ. Sch. Med., Dep. Neurosci., WBSB 908, 725 N. Wolfe St., Baltimore, MD 21205 USA
SOURCE: Journal of Cell Biology, (1995) Vol. 131, No. 5, pp. 1149-1161.
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DOCUMENT TYPE: Article
LANGUAGE: English

AB Oxidative stress has been proposed as a common mediator of apoptotic death. To investigate further the role of oxidants in this process we have studied the effects of antioxidants on Sindbis virus (SV) induced apoptosis in two cell lines, AT-3 (a prostate carcinoma line) and N18 (a neuroblastoma line). The thiol antioxidant, N-acetylcysteine (NAC), at concentrations above 30 mM, completely abrogates SV-induced apoptosis in AT-3 and N18 cells. The effects of NAC cannot be attributed to inhibition of viral entry or viral replication, changes in extracellular osmolarity or to increases in cellular glutathione levels, nor can they be mimicked by chelators of trace metals, inhibitors of lipid peroxidation or peroxide scavengers. In contrast other thiol agents including pyrrolidine dithiocarbamate (PDTC, 75 mu-M) are protective. Because NAC and PDTC are among the most effect inhibitors of the **transcription factor** NF-kappa B, we examined SV's ability to active NF-kappa B before the onset of morphologic or biochemical evidence of apoptosis. Within hours of infection, SV induced a robust increase in nuclear NF-kappa B activity in AT-3 and N18 cells; this activation was suppressible by NAC and PDTC. Overexpression of bcl-2 in AT-3 cells, which has been shown to inhibit SV-induced apoptosis, also inhibits SV-induced NF-kappa B activation. To determine if NF-kappa B activation is necessary for SV-induced apoptosis in these cells, we used double stranded oligonucleotides with consensus NF-kappa B sequences as **transcription factor** decoys (TFDs) to inhibit NF-kappa B **binding** to native DNA sites. Wild-type, but not mutant. TFDs inhibit SV-induced apoptosis in AT-3 cells. In contrast, TFD inhibition of NF-kappa B nuclear activity in N18 cells did not prevent SV-induced apoptosis. Taken together, these observations define a cell type-specific, **transcription factor** signaling pathway necessary for SV-induced apoptosis. Understanding the precise mechanism by which Bcl-2 and thiol agents inhibit SV-induced nuclear NF-kappa B activity in AT-3 cell may provide insights into the pluripotent anti- apoptotic actions of these agents.

L4 ANSWER 40 OF 123 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:367322 BIOSIS
DOCUMENT NUMBER: PREV199598381622
TITLE: A gene therapy strategy using a **transcription factor decoy** of the E2F **binding** site inhibits smooth muscle proliferation in vivo.
AUTHOR(S): Morishita, Ryuichi; Gibbons, Gary H.; Horiuchi, Masatsugu; Ellison, Kristin E.; Nakajima, Masatoshi; Zhang, Lunan; Kaneda, Yasufumi; Ogihara, Toshio; Dzau, Victor J. (1)
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SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 13, pp. 5855-5859.
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DOCUMENT TYPE: Article
LANGUAGE: English
AB The application of DNA technology to regulate the transcription of disease-related genes in vivo has important therapeutic potentials. The **transcription factor** E2F plays a pivotal role in the coordinated transactivation of cell cycle-regulatory genes such as c-myc, cdc2, and the gene encoding proliferating-cell nuclear antigen (PCNA) that are involved in lesion formation after vascular injury. We hypothesized that double-stranded DNA with high affinity for E2F may be introduced in vivo as a **decoy** to bind E2F and block the activation of genes mediating cell cycle progression and intimal hyperplasia after vascular injury. Gel mobility-shift assays showed complete competition for E2F **binding** protein by the E2F **decoy**. Transfection with E2F **decoy** inhibited expression of c-myc, cdc2, and the PCNA gene as well as vascular smooth muscle cell proliferation both in vitro and in the in vivo model of rat carotid injury. Furthermore, 2 weeks after in vivo transfection, neointimal formation was significantly prevented by the E2F **decoy**, and this inhibition continued up to 8 weeks after a single transfection in a dose-dependent manner. Transfer of an E2F **decoy** can therefore modulate gene expression and inhibit smooth muscle proliferation and vascular lesion formation in vivo.